Scientific letter

Percutaneous atrioseptostomy for left ventricular unloading in pediatric patients in cardiogenic shock on venoarterial ECMO support

Septostomía auricular percutánea de descarga ventricular izquierda en pacientes pediátricos en shock *cardiogénico asistidos con ECMO venoarterial*

To the Editor,

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is the main circulatory assistance technique for cardiogenic shock in the pediatric population.[1] To avoid congestion and distension of the left heart and consequent pulmonary edema, a drainage system is required to facilitate ventricular rest and recovery. One such drainage technique is percutaneous atrial septostomy (PAS).[2,3]

In our hospital, urgent PAS is performed as standard for all patients with severe ventricular dysfunction who require VA-ECMO support. We report a series of 16 patients who were admitted to our hospital between 2015 and 2020 in cardiogenic shock and requiring VA-ECMO support. Peripheral cannulation of the neck (right jugular vein and carotid artery) was used for ECMO in all patients, with subsequent surgical repair in most. Once stabilized on ECMO, the patients were transferred to the cardiac catheterization laboratory for PAS. During the procedure, we took the opportunity to take an endomyocardial biopsy in selected patients.

The PAS technique is carried out, if there is vascular availability, with double venous access. Via one access line, a snare is placed in the inferior vena cava; via the other access line, the PAS material is placed, which is passed through the snare.[4] If the foramen ovale is not patent, PAS is performed with a Brockenbrough needle under transesophageal echocardiographic guidance (video 1 of supplementary data). The selection of the type and size of stent is influenced by several factors: left atrial pressure (the main factor), inotropic support, and aortic valve opening. With higher left atrial pressure, more inotropic support, and a closed valve, the diameter of the stent should be closer to half the length of the septum; in the opposite situation, closer to a third. In target diameters of up to 10 mm, a 10 × 19 Palmaz Genesis stent (Cordis Corp, USA) is used; in larger diameters, a Cheatham-Platinum stent (NuMED Inc, USA) is used. The snare is moved until it touches the interatrial septum, marking where the center of the final position of the stent (video 2 of the supplementary data); when it is tensed during inflation, this gives the stent a slight hourglass shape and better stability (video 3 of the supplementary data). At the end of the procedure, the absence of a hemodynamic gradient between the atria is checked to confirm that the correct stent diameter has been chosen.

Statistical analysis was performed using R Core Team version 2016 (R: A language and environment for statistical computing, R Foundation for Statistical Computing, Austria). Continuous variables are presented as median (range), and categorical variables, as frequency. The Wilcoxon test was used for the difference in left atrial pressures after the procedure. P values $< .05$ were considered statistically significant.

The characteristics of the patients and the procedure are described in table 1 and table 2. An interatrial stent was inserted in all patients except 1 neonate, who underwent PAS with balloon only, as the left atrial pressures were not significantly high and

Table 1
Overall characteristics of the patients and procedure

Patient characteristics			Procedure details		
Sex	Men	6	Access	Double access	9
	Women	10		Single access	7
Age		6.8 years [10 d-15 y]	Septum length, mm		28 [11-49]
Weight, kg		17.5 [2.5-77]	Stent implanted		15
Diagnosis	Myocarditis	8	Type of stent	PG 19×10	7
	Inherited DCM	4		PG 25×10	1
	Idiopathic DCM	4		CP 34 mm	5
				CP 28 mm	2
Outcome	Recovery	8	Stent diameter, mm		11 [10-20]
	Transplant	6			
	Death	2			
ECMO, days		18 [7-78]	Endomyocardial biopsy		11
Time admission-ECMO, h		11.5 [3-288]	Dilatation of stent		2
Time ECMO-stent, h		5.8 [3-12.9]	Procedural time, min	Stent and biopsy	101 [68-147]
				Stent	67 [29-137]
			Fluoroscopy time, min	Stent and biopsy	34 [17-63]
				Stent	19 [10-43]

CP, Cheatham-Platinum stent (NuMED Inc, USA); DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenator; LAP, left atrial pressure; PG, Palmaz Genesis stent (Cordis Corp, USA).
Values are expressed as No. (%), mean ± standard deviation or median [range].

Table 2
Individual characteristics of the patients and procedure

	Age, y	Sex	Weight, kg	Diagnosis	Time ECMO-stent, h	Access	Initial LAP, mmHg	Type of stent	Diameter, mm	EMB	ECMO duration, d	Outcome
1	15	M	55	DCM	7:58	Double	39	CP 34	16	Yes	18	Transplant
2	8	F	18	DCM	6:55	Double	26	CP 28	14	Yes	20	Transplant
3	5	M	17	DCM	6:35	Double		CP 34	16	No	7	Transplant
4	9	F	40	DCM	5:24	Double	35	CP 34	20	Yes	78	Transplant
5	0.16	F	4	DCM	3:02	Single	8	PG 10×19	10	No	29	Transplant
6	7	F	19	Myocarditis	4:16	Double	13	PG 10×19	10	Yes	7	Recovery
7	0.83	F	8	DCM	6:42	Single	32	PG 10×19	10	Yes	27	Recovery
8	0.75	M	9	Myocarditis	4:32	Single		PG 10×19	10	Yes	18	Recovery
9	2	M	13	Myocarditis	3:34	Single	9	PG 10×19	10	Yes	17	Recovery
10	9	F	30	Myocarditis	9:14	Double	11	CP 28	12	Yes	69	Recovery
11	2	M	15	Myocarditis	5:40	Single		PG 10×19	10	No	7	Death
12	0.02	F	2.5	Myocarditis	5:54	Single	15	No stent		No	16	Death
13	0.08	F	3.6	DCM	6:13	Single	33	PG 10×19	10	No	36	Transplant
14	15	M	77	DCM	5:31	Double	34	CP 34	19	Yes	23	Recovery
15	7	F	20	Myocarditis	5:08	Double	11	PG 25×10	11	Yes	15	Recovery
16	11	F	47	Myocarditis	12:58	Double	11	CP 34	15	Yes	7	Recovery

CP, Cheatham-Platinum stent (NuMED Inc., USA); DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenator; EMB, endomyocardial biopsy; F, female; LAP, left atrial pressure; PG, Palmaz Genesis stent (Cordis Corp.,USA); M, male.

there was a ventricular septal defect. In the same procedure, we took an endomyocardial biopsy for diagnostic purposes from 11 patients; this was not done in 5 due to a low probability of myocarditis or high risk due to very low weight. One limitation is that we did not keep a record of all the pressures measured, so information on initial final values of left atrial pressure was available for review in only 8 patients. In these patients, a significant decrease was confirmed, with a median −16.5 mmHg (95% confidence interval, 23-5.5 mmHg; $P = .02$). Based on experience from earlier series, showing a reduction in ECMO time associated with early PAS,[5] our protocol recommends urgent PAS after starting ECMO to favor early resolution of pulmonary edema, faster ventricular recovery, and shorter duration of ECMO, with a median 5.8 (3-12.9) hours between starting ECMO and PAS completion. All the patients had pulmonary edema, which resolved after PAS. At 14 days and 62 days, 2 patients returned to the catheterization laboratory due to recurrent pulmonary edema to rule out stent stenosis, and low hemodynamic gradients were observed (2-3 mmHg), with high biventricular filling pressures that explained the recurrence of edema. The stent was dilated to eliminate the gradient, then diastolic failure and venous congestion were treated, with clinical improvement. No complications associated with the procedure were observed in any of the patients.

At follow-up (median 16.8 [0.3-54.2] months), of the 8 patients who recovered ventricular function, we observed mild right heart dilatation in 5 patients—median Z-score +2.3 (0.4-4.3)—secondary to a left-to-right shunt produced by the interatrial stent; so far this has not required closure. As this group comprised essentially patients with a defect diameter of 10 mm, which over time will tend to get smaller due to neointimal growth in the stent, it is reasonable to assume that at least some of the defects may become insignificant over time and will not require percutaneous closure, although, given the support guaranteed by the stent, it seems likely such a procedure would be technically very simple.

The percutaneous creation of a nonrestrictive atrial septal defect is a safe and effective solution to the problem of left heart drainage in patients with cardiogenic shock requiring VA-ECMO, and also allows endomyocardial biopsy during the same procedure when indicated.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.1016/j.rec.2021.01.010

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A novel genetic variant in the NM_000169.2 region of the *GLA* gene (p.Gly163*) responsible for Fabry disease

Una nueva variante genética en la región NM_000169.2 del gen GLA *(p.Gly163*) causante de la enfermedad de Fabry*

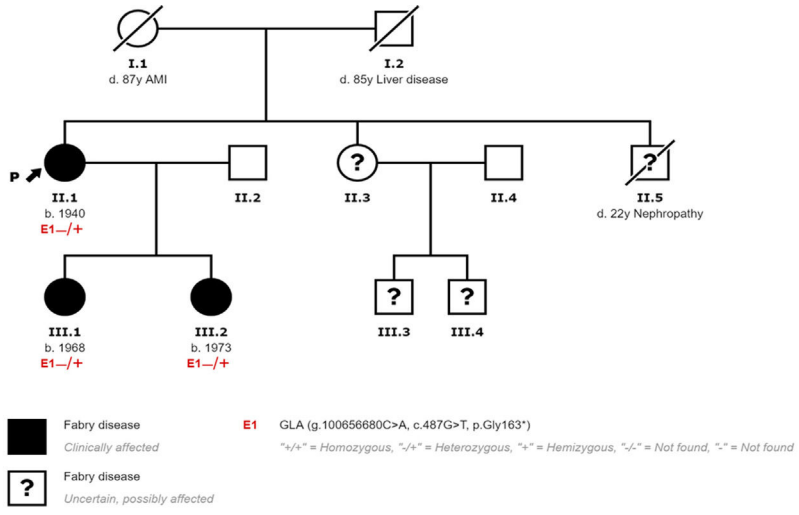
To the Editor,

Fabry disease (FD) is a rare, progressive lysosomal storage disorder caused by a functional deficiency of the lysosomal α-galactosidase enzyme (α-gal A).[1] It is an X-chromosome inheritance-linked disorder caused by pathogenic genetic variants in the *GLA* gene. These produce a functional enzyme deficiency, provoking intracellular accumulation of glycosphingolipids, predominantly globotriaosylceramide (lyso-Gb3) in lysosomal and nonlysosomal compartments of the skin, heart, kidney, brain, and other tissue cells, which contributes to the multisystemic manifestation of this disorder and early patient death.[1,2]

Fabry disease was first described among male patients with a severe form of the disease, a clinical phenotype now known as the classic form of the disease.[1,2] These patients are usually carriers of nonsense or frameshift genetic variants that generate an absence of, or severely reduced, α-gal A activity, with symptom onset during infancy or adolescence, progressive failure in multiple organs and, finally, early death.[1–3] However, a much larger group of patients are usually carriers of other genetic variants that do not cause such large changes in the protein structure (such as the majority of missense mutations) and give rise to variable levels of residual α-gal A activity, which might explain the late onset, less severe phenotypes encountered in the phenotypic expression of the disorder.[3]

Women are heterozygous for genetic variants in the *GLA* gene and manifest a heterogeneous clinical spectrum that varies between the absence of symptoms and a severity similar to that of male patients. Severity depends in part on the genetic variant and the pattern of X-chromosome inactivation, known as lyonization, which is a random process. Therefore, heterozygous patients who predominantly express a nonmutated GLA allele experience few or no symptoms, whereas patients who predominantly express a mutated GLA allele may experience a progression of the disorder similar to the masculine phenotypes, whether in a classic or late-onset form, depending on the underlying genetic variant in their family.[4] Through this random inactivation of the mutated allele, in women α-galactosidase and lyso-Gb3 activity could show normal values.

A



B

Measurements	Subject II.1	Subject III.1	Subject III. 2
α-Galactosidase activity in plasma (May 2018) [Normal values 2.5-8 µmol/L/h]	5.2	0.5	1
α-Galactosidase activity in dry drop (June 2018) [Normal values 2.1-1.4 µmol/L/h]	2.1	0.1	0.3
Lyso-Gb3 in dry drop [Normal values 0-1.4 ng/mL]			
May 2018	1.2	3.63	1.94
March 2019		2.98	2.75
July 2019		3.11	2.63

Figure 1. A: family diagram with the cases studied to date. B: measurements of enzyme activity and levels of Lyso-Gb3 in the follow-up.